

WHAT WE CLAIM IS:

1. A method for the treatment or prophylaxis of one or more aldosterone-mediated pathogenic effects in a human subject suffering from or susceptible to the pathogenic effect or effects, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, wherein the subject has one or more conditions selected from the group consisting of a sub-normal endogenous aldosterone level, salt sensitivity and an elevated dietary sodium intake, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

2. The method of Claim 1 wherein the subject has a sub-normal endogenous aldosterone level.

3. The method of Claim 2 wherein the pathogenic effect is selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, baroreceptor dysfunction, migraine headaches, hot flashes, and premenstrual tension.

4. The method of Claim 2 wherein the pathogenic effect is cardiovascular disease.

5. The method of Claim 2 wherein the pathogenic effect is renal dysfunction.

6. The method of Claim 2 wherein the pathogenic effect is edema.

7. The method of Claim 2 wherein the pathogenic effect is insulinopathy.

8. The method of Claim 2 wherein the pathogenic effect is heart failure.

9. The method of Claim 2 wherein the pathogenic effect is stroke.

10. The method of Claim 2 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

- (f) the subject is a non-modulating individual; or
- (g) the subject has or is susceptible to one or more conditions selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;
- (h) the subject is at least 55 years of age; or
- (i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or
- (j) the subject has one or more genetic markers associated with salt sensitivity; or
- (k) the subject has one or more 1st, 2nd, or 3rd degree relatives who are or were salt sensitive; or
- (l) the subject has greater than about 25% body fat.

11. The method of Claim 2 wherein the subject has or is susceptible to cardiovascular disease.

12. The method of Claim 2 wherein the subject has or is susceptible to renal dysfunction.

13. The method of Claim 2 wherein the subject has or is susceptible to heart failure.

14. The method of Claim 2 wherein the subject is insulin

resistant.

15. The method of Claim 2 wherein the subject has suffered a stroke.

16. The method of Claim 2 wherein the subject is greater than about 55 years of age.

17. The method of Claim 2 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

18. The method of Claim 2 wherein the subject is, in whole or in part, a member of the Black ethnic group.

19. The method of claim 2 wherein the subject has a sub-normal level of urinary aldosterone.

20. The method of claim 2 wherein the subject has a sub-normal level of serum aldosterone.

21. The method of Claim 2 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of sodium.

22. The method of Claim 2 wherein the pathogenic effect

results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

23. The method of Claim 2 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the brain.

24. The method of Claim 23 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

25. The method of Claim 24 wherein the pathogenic effect is selected from hypertension and stroke.

26. The method of Claim 2 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the kidney.

27. The method of Claim 26 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

28. The method of Claim 27 wherein the pathogenic effect is selected from renal hypertension and nephrosclerosis.

29. The method of Claim 2 wherein the pathogenic effect results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

30. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a cardioprotective-effective amount.

31. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a renal protective-effective amount.

32. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a non-diuresis-effective amount.

33. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

34. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

35. The method of Claim 2 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

36. The method of Claim 2 wherein the epoxy-steroidal

compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

37. The method of Claim 2 wherein the epoxy-steroidal compound is eplerenone.

38. The method of Claim 1 wherein the subject has salt sensitivity.

39. The method of Claim 38 wherein the subject is determined to be salt sensitive by means of a salt challenge test.

40. The method of Claim 38 wherein the subject exhibits an increase in systolic blood pressure or diastolic blood pressure, or both, of at least about 5% when daily sodium chloride intake by the subject is increased from less than about 3 g/day to at least about 10 g/day.

41. The method of Claim 38 wherein the pathogenic effect is selected from hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, baroreceptor dysfunction, migraine headaches, hot flashes, and premenstrual tension.

42. The method of Claim 38 wherein the pathogenic effect is cardiovascular disease.

43. The method of Claim 38 wherein the pathogenic effect is renal dysfunction.

44. The method of Claim 38 wherein the pathogenic effect is edema.

45. The method of Claim 38 wherein the pathogenic effect is insulinopathy.

46. The method of Claim 38 wherein the pathogenic effect is heart failure.

47. The method of Claim 38 wherein the pathogenic effect is stroke.

48. The method of Claim 38 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a urinary sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

(f) the subject is a non-modulating individual; or

(g) the subject has or is susceptible to one or more conditions selected from the group consisting of hypertension, cardiovascular

disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;

(h) the subject is at least 55 years of age; or

(i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or

(j) the subject has one or more genetic markers associated with salt sensitivity; or

(k) the subject has one or more 1st, 2nd, or 3rd degree relatives who are or were salt sensitive; or

(l) the subject has greater than about 25% body fat.

49. The method of Claim 38 wherein the subject has or is susceptible to cardiovascular disease.

50. The method of Claim 38 wherein the subject has or is susceptible to renal dysfunction.

51. The method of Claim 38 wherein the subject has or is susceptible to heart failure.

52. The method of Claim 38 wherein the subject is insulin resistant.

53. The method of Claim 38 wherein the subject has suffered

a stroke.

54. The method of Claim 38 wherein the subject is greater than about 55 years of age.

55. The method of Claim 38 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

56. The method of Claim 38 wherein the subject is, in whole or in part, a member of the Black ethnic group.

57. The method of Claim 38 wherein the subject has an average daily intake of sodium of at least about 50 milliequivalents.

58. The method of Claim 38 wherein the subject has an average daily intake of sodium of at least about 100 milliequivalents.

59. The method of Claim 38 wherein the subject has an average daily intake of sodium of at least about 150 milliequivalents.

60. The method of Claim 38 wherein the subject has an average daily intake of sodium of at least about 200 milliequivalents.

61. The method of Claim 38 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the

presence of an elevated level of sodium.

62. The method of Claim 38 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

63. The method of Claim 38 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the brain.

64. The method of Claim 63 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

65. The method of Claim 64 wherein the pathogenic effect is selected from hypertension and stroke.

66. The method of Claim 38 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the kidney.

67. The method of Claim 66 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

68. The method of Claim 67 wherein the pathogenic effect is selected from renal hypertension and nephrosclerosis.

69. The method of Claim 38 wherein the pathogenic effect results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

70. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is an antihypertensive-effective amount.

71. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a cardioprotective-effective amount.

72. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a renal protective-effective amount.

73. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a non-diuresis-effective amount.

74. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

75. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

76. The method of Claim 38 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

77. The method of Claim 38 wherein the epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-;

;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

78. The method of Claim 38 wherein the epoxy-steroidal compound is eplerenone.

79. The method of Claim 1 wherein the subject has an elevated dietary sodium intake.

80. The method of Claim 79 wherein the pathogenic effect is selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, baroreceptor dysfunction, migraine headaches, hot flashes, and premenstrual tension.

81. The method of Claim 79 wherein the pathogenic effect is cardiovascular disease.

82. The method of Claim 79 wherein the pathogenic effect is renal dysfunction.

83. The method of Claim 79 wherein the pathogenic effect is edema.

84. The method of Claim 79 wherein the pathogenic effect is insulinopathy.

85. The method of Claim 79 wherein the pathogenic effect is heart failure.

86. The method of Claim 79 wherein the pathogenic effect is stroke.

87. The method of Claim 79 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a urinary sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

(f) the subject is a non-modulating individual; or

(g) the subject has or is susceptible to one or more conditions selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;

- (h) the subject is at least 55 years of age; or
- (i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or
- (j) the subject has one or more genetic markers associated with salt sensitivity; or
- (k) the subject has one or more 1st, 2nd, or 3rd degree relatives who are or were salt sensitive; or
- (l) the subject has greater than about 25% body fat.

88. The method of Claim 79 wherein the subject has or is susceptible to cardiovascular disease.

89. The method of Claim 79 wherein the subject has or is susceptible to renal dysfunction.

90. The method of Claim 79 wherein the subject has or is susceptible to heart failure.

91. The method of Claim 79 wherein the subject is insulin resistant.

92. The method of Claim 79 wherein the subject has suffered a stroke.

93. The method of Claim 79 wherein the subject is greater than about 55 years of age.

94. The method of Claim 79 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

95. The method of Claim 79 wherein the subject is, in whole or in part, a member of the Black ethnic group.

96. The method of Claim 79 wherein the subject has an average daily intake of sodium of at least about 50 milliequivalents.

97. The method of Claim 79 wherein the subject has an average daily intake of sodium of at least about 100 milliequivalents.

98. The method of Claim 79 wherein the subject has an average daily intake of sodium of at least about 150 milliequivalents.

99. The method of Claim 79 wherein the subject has an average daily intake of sodium of at least about 200 milliequivalents.

100. The method of Claim 79 wherein the subject has salt sensitivity.

101. The method of Claim 79 wherein the pathogenic effect

results, in whole or in part, from the action of aldosterone in the presence of an elevated level of sodium.

102. The method of Claim 79 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

103. The method of Claim 79 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the brain.

104. The method of Claim 103 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

105. The method of Claim 104 wherein the pathogenic effect is selected from hypertension and stroke.

106. The method of Claim 79 wherein the pathogenic effect is mediated, in whole or in part, by aldosterone present in the kidney.

107. The method of Claim 106 wherein the pathogenic effect results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

108. The method of Claim 107 wherein the pathogenic effect is selected from renal hypertension and nephrosclerosis.

109. The method of Claim 79 wherein the pathogenic effect results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

110. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is an antihypertensive-effective amount.

111. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a cardioprotective-effective amount.

112. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a renal protective-effective amount.

113. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a non-diuresis-effective amount.

114. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

115. The method of Claim 79 wherein the therapeutically-

effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

116. The method of Claim 79 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

117. The method of Claim 79 wherein the epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, ($7\alpha, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, ($7\alpha, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, ($7\alpha, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, ($7\alpha, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, ($6\beta, 7\beta, 11\alpha$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

118. The method of Claim 79 wherein the epoxy-steroidal compound is eplerenone.

119. A method for the treatment or prophylaxis of hypertension in a human subject suffering from or susceptible to hypertension, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, wherein the subject has salt sensitivity or an elevated dietary sodium intake, or both, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

120. The method of Claim 119 wherein the subject is determined to be salt sensitive by means of a salt challenge test.

121. The method of Claim 119 wherein the subject exhibits an increase in systolic blood pressure or diastolic blood pressure, or both, of at least about 5% when daily sodium chloride intake by the subject is increased from less than about 3 g/day to at least about 10 g/day.

122. The method of Claim 119 wherein the subject has an

average daily intake of sodium of at least about 50 milliequivalents.

123. The method of Claim 119 wherein the subject has an average daily intake of sodium of at least about 100 milliequivalents.

124. The method of Claim 119 wherein the subject has an average daily intake of sodium of at least about 150 milliequivalents.

125. The method of Claim 119 wherein the subject has an average daily intake of sodium of at least about 200 milliequivalents.

126. The method of Claim 119 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a urinary sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

(f) the subject is a non-modulating individual; or

(g) the subject has or is susceptible to one or more conditions

selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;

(h) the subject is at least 55 years of age; or

(i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or

(j) the subject has one or more genetic markers associated with salt sensitivity; or

(k) the subject has one or more 1st, 2nd, or 3rd degree relatives who are or were salt sensitive; or

(l) the subject has greater than about 25% body fat.

127. The method of Claim 119 wherein the subject has or is susceptible to cardiovascular disease.

128. The method of Claim 119 wherein the subject has or is susceptible to heart failure.

129. The method of Claim 119 wherein the subject has suffered a stroke.

130. The method of Claim 119 wherein the subject is insulin resistant.

131. The method of Claim 119 wherein the subject is greater than about 55 years of age.

132. The method of Claim 119 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

133. The method of Claim 119 wherein the subject is, in whole or in part, a member of the Black ethnic group.

134. The method of Claim 119 wherein the hypertension results, in whole or in part, from the action of aldosterone in the presence of an elevated level of sodium.

135. The method of Claim 119 wherein the hypertension results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

136. The method of Claim 119 wherein the hypertension is mediated, in whole or in part, by aldosterone present in the brain.

137. The method of Claim 136 wherein the hypertension results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

138. The method of Claim 119 wherein the hypertension is mediated, in whole or in part, by aldosterone present in the kidney.

139. The method of Claim 138 wherein the hypertension results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

140. The method of Claim 119 wherein the hypertension results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

141. The method of Claim 119 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

142. The method of Claim 119 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

143. The method of Claim 119 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

144. The method of Claim 119 wherein the epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

145. The method of Claim 119 wherein the epoxy-steroidal compound is eplerenone.

146. A method for the treatment or prophylaxis of cardiovascular disease in a human subject suffering from or susceptible to cardiovascular disease, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, wherein the subject has salt

sensitivity or an elevated dietary sodium intake, or both, and where in the epoxy-steroidal compounds are aldosterone antagonists.

147. The method of Claim 146 wherein the cardiovascular disease is heart failure.

148. The method of Claim 146 wherein the subject is determined to be salt sensitive by means of a salt challenge test.

149. The method of Claim 146 wherein the subject exhibits an increase in systolic blood pressure or diastolic blood pressure, or both, of at least about 5% when daily sodium chloride intake by the subject is increased from less than about 3 g/day to at least about 10 g/day.

150. The method of Claim 146 wherein the subject has an average daily intake of sodium of at least about 50 milliequivalents.

151. The method of Claim 146 wherein the subject has an average daily intake of sodium of at least about 100 milliequivalents.

152. The method of Claim 146 wherein the subject has an average daily intake of sodium of at least about 150 milliequivalents.

153. The method of Claim 146 wherein the subject has an average daily intake of sodium of at least about 200 milliequivalents.

154. The method of Claim 146 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a urinary sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

(f) the subject is a non-modulating individual; or

(g) the subject has or is susceptible to one or more conditions selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;

(h) the subject is at least 55 years of age; or

(i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or

(j) the subject has one or more genetic markers associated with salt sensitivity; or

(k) the subject has one or more 1st, 2nd, or 3rd degree relatives

who are or were salt sensitive; or

(l) the subject has greater than about 25% body fat.

155. The method of Claim 146 wherein the subject has or is susceptible to hypertension.

156. The method of Claim 146 wherein the subject has suffered a stroke.

157. The method of Claim 146 wherein the subject is insulin resistant.

158. The method of Claim 146 wherein the subject is greater than about 55 years of age.

159. The method of Claim 146 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

160. The method of Claim 146 wherein the subject is, in whole or in part, a member of the Black ethnic group.

161. The method of Claim 146 wherein the cardiovascular disease results, in whole or in part, from the action of aldosterone in the presence of an elevated level of sodium.

162. The method of Claim 146 wherein the cardiovascular disease results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

163. The method of Claim 146 wherein the cardiovascular disease is mediated, in whole or in part, by aldosterone present in the brain.

164. The method of Claim 163 wherein the cardiovascular disease results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

165. The method of Claim 146 wherein the cardiovascular disease is mediated, in whole or in part, by aldosterone present in the kidney.

166. The method of Claim 165 wherein the cardiovascular disease results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

167. The method of Claim 146 wherein the cardiovascular disease results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

168. The method of Claim 146 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a cardioprotective-effective amount.

169. The method of Claim 146 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a non-diuresis-effective amount.

170. The method of Claim 146 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

171. The method of Claim 146 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

172. The method of Claim 146 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

173. The method of Claim 146 wherein the epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7] pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

174. The method of Claim 146 wherein the epoxy-steroidal compound is eplerenone.

175. A method for the treatment or prophylaxis of heart failure in a human subject suffering from or susceptible to cardiovascular disease, the method comprising administering to the subject a therapeutically-effective amount of an ACE inhibitor, a loop diuretic, and one or more epoxy-steroidal compounds, wherein the subject has salt sensitivity or an elevated dietary sodium intake, or both, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

176. The method of Claim 175 wherein the subject is determined to be salt sensitive by means of a salt challenge test.

177. The method of Claim 175 wherein the subject exhibits an increase in systolic blood pressure or diastolic blood pressure, or both, of at least about 5% when daily sodium chloride intake by the subject is increased from less than about 3 g/day to at least about 10 g/day.

178. The method of Claim 175 wherein the subject has an average daily intake of sodium of at least about 50 milliequivalents.

179. The method of Claim 175 wherein the subject has an average daily intake of sodium of at least about 100 milliequivalents.

180. The method of Claim 175 wherein the subject has an average daily intake of sodium of at least about 150 milliequivalents.

181. The method of Claim 175 wherein the subject has an average daily intake of sodium of at least about 200 milliequivalents.

182. The method of Claim 175 wherein the subject satisfies at least one or more of the following conditions:

(a) the subject has an activities ratio of plasma aldosterone (ng/dL) to plasma renin (ng/ml/hr) greater than about 30; or

(b) the subject has a morning plasma renin level less than or

equal to about 1.0 ng/dL/hr; or

(c) the subject has a systolic blood pressure greater than about 130 mm Hg or a diastolic blood pressure greater than about 85 mm Hg, or both; or

(d) the subject has a urinary sodium to potassium ratio less than about 6; or

(e) the subject has an elevated plasma level of one or more endothelins; or

(f) the subject is a non-modulating individual; or

(g) the subject has or is susceptible to one or more conditions selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, and endothelial dysfunction;

(h) the subject is at least 55 years of age; or

(i) the subject is, in whole or in part, a member of at least one ethnic group selected from the Japanese ethnic group, the American Indian ethnic group, and the Black ethnic group; or

(j) the subject has one or more genetic markers associated with salt sensitivity; or

(k) the subject has one or more 1st, 2nd, or 3rd degree relatives who are or were salt sensitive; or

(l) the subject has greater than about 25% body fat.

183. The method of Claim 175 wherein the subject has or is susceptible to hypertension.

184. The method of Claim 175 wherein the subject is insulin resistant.

185. The method of Claim 175 wherein the subject is greater than about 55 years of age.

186. The method of Claim 175 wherein the subject is, in whole or in part, a member of the Japanese ethnic group.

187. The method of Claim 175 wherein the subject is, in whole or in part, a member of the Black ethnic group.

188. The method of Claim 175 wherein the heart failure results, in whole or in part, from the action of aldosterone in the presence of an elevated level of sodium.

189. The method of Claim 175 wherein the heart failure results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

190. The method of Claim 175 wherein the heart failure is mediated, in whole or in part, by aldosterone present in the brain.

191. The method of Claim 190 wherein the heart failure results, in whole or in part, from the action of aldosterone in the

presence of an elevated level of intracellular sodium.

192. The method of Claim 175 wherein the heart failure is mediated, in whole or in part, by aldosterone present in the kidney.

193. The method of Claim 192 wherein the heart failure results, in whole or in part, from the action of aldosterone in the presence of an elevated level of intracellular sodium.

194. The method of Claim 175 wherein the heart failure results, in whole or in part, from the combined action of aldosterone and elevated dietary sodium intake in the subject.

195. The method of Claim 175 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a cardioprotective-effective amount.

196. The method of Claim 175 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is a non-diuresis-effective amount.

197. The method of Claim 175 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day.

198. The method of Claim 175 wherein the therapeutically-

effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

199. The method of Claim 175 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

200. The method of Claim 175 wherein the epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, ($7\alpha, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, ($7\alpha, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, 7-(1-methylethyl) ester, monopotassium salt, ($7\alpha, 11\alpha, 17\beta$)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, ($7\alpha, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, ($6\beta, 7\beta, 11\alpha$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, ($6\beta, 7\beta, 11\alpha, 17\beta$)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-; and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α , 11 α , 17 β)-.

201. The method of Claim 175 wherein the epoxy-steroidal compound is eplerenone.

202. A method for the prophylaxis of one or more aldosterone-mediated pathogenic effects in a human subject suffering from or susceptible to the pathogenic effect or effects, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds,

wherein the pathogenic effect or effects are selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, baroreceptor dysfunction, migraine headaches, hot flashes, and and premenstrual tension;

wherein the subject has one or more conditions selected from the group consisting of a sub-normal endogenous aldosterone level, salt sensitivity and an elevated dietary sodium intake; and

wherein the epoxy-steroidal compounds are aldosterone antagonists.

203. The method of Claim 202 wherein the epoxy-steroidal

compound is eplerenone.

204. A method for the treatment or prophylaxis of salt sensitivity in a human subject in need thereof, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

205. The method of Claim 204 wherein the epoxy-steroidal compound is eplerenone.

206. A method for reducing sodium appetite in a human subject in need thereof, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

207. The method of Claim 206 wherein the epoxy-steroidal compound is eplerenone.

208. A method for reducing or reversing the progression of salt sensitivity in a human subject suffering from or susceptible to salt sensitivity, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

209. The method of Claim 208 wherein the epoxy-steroidal compound is eplerenone.

210. A method for the treatment or prophylaxis of a human subject to reduce or prevent one or more pathogenic effects resulting, in whole or in part, from aberrant aldosterone levels in brain, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, wherein the subject has salt sensitivity or an elevated dietary sodium intake, or both, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

211. The method of Claim 210 wherein the epoxy-steroidal compound is eplerenone.

212. A method for the treatment or prophylaxis of a human subject to reduce or prevent one or more pathogenic effects resulting, in whole or in part, from aberrant sodium retention in the kidney, the method comprising administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compounds, wherein the subject has salt sensitivity or an elevated dietary sodium intake, or both, and wherein the epoxy-steroidal compounds are aldosterone antagonists.

213. The method of Claim 212 wherein the epoxy-steroidal compound is eplerenone.

214. A method for the treatment of salt sensitive hypertension in a human subject in need thereof, the method comprising administering to the subject an therapeutically-effective amount of eplerenone.

215. A method for the treatment of salt sensitive heart failure in a human subject in need thereof, the method comprising administering to the subject a therapeutically-effective amount of eplerenone.